

THE CLAIMS

What is claimed is:

1. A dosage form comprising an adsorbent and an adverse agent, wherein at least a majority of the adverse agent is adsorbed onto the adsorbent.
- 5 2. The dosage form of claim 1, wherein at least 80 wt.% of the adverse agent is adsorbed onto the adsorbent.
3. The dosage form of claim 2, wherein at least 90 wt.% of the adverse agent is adsorbed onto the adsorbent.
- 10 4. The dosage form of claim 1, wherein the adsorbent comprises at least one material selected from the group consisting of activated charcoal, alumina, silicon dioxide bentonite, kaolin, and mixtures of any two or more of the foregoing.
5. The dosage form of claim 4, wherein the adsorbent is activated charcoal.
6. The dosage form of claim 1, further comprising at least one hydrophobic material disposed at least on a portion of the outer surface of the adsorbent.
- 15 7. The oral dosage form of claim 6, wherein the at least one hydrophobic material is selected from the group consisting of acrylic and methacrylic acid polymers and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes, fatty alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides, hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon
20 backbones, and mixtures of any two or more of the foregoing.
8. The dosage form of claim 7, wherein the at least one hydrophobic material is selected from the group consisting of glyceryl monostearate; beeswax; cetyl alcohol; stearyl alcohol; hydrogenated castor oil; hydrogenated cottonseed oil; stearyl alcohol; stearic acid; and mixtures of any two or more of the foregoing.
- 25 9. The dosage form of claim 1, wherein the dosage form is an oral dosage form.

10. The dosage form of claim 1, wherein the dosage form releases about 0.5 mg or less of the adverse agent *in vivo* following intact administration.

11. The dosage form of claim 1, wherein the dosage form releases about 0.05 mg or less of the adverse agent *in vivo* following intact administration.

5 12. A dosage form comprising:
a plurality of first particles comprising an active agent; and
a plurality of second particles comprising an adsorbent and an adverse agent;
wherein
at least a majority of the adverse agent is adsorbed onto the adsorbent.

10 13. The dosage form of claim 12, wherein the adsorbent is selected from the group consisting of activated charcoal, alumina, bentonite, kaolin, and mixtures of any two or more of the foregoing.

14. The dosage form of claim 13, wherein the adsorbent is activated charcoal.

15 15. The dosage form of claim 12, wherein the plurality of second particles further comprise at least one hydrophobic material disposed on at least a portion of the outer surface of the adsorbent.

16. The dosage form of claim 15, wherein the at least one hydrophobic material is selected from the group consisting of acrylic and methacrylic acid polymers and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes,
20 fatty alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides, hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon backbones, and mixtures of any two or more of the foregoing.

17. The dosage form of claim 16, wherein the at least one hydrophobic material is selected from the group consisting of glyceryl monostearate; beeswax; cetyl
25 alcohol; stearyl alcohol; hydrogenated castor oil; hydrogenated cottonseed oil; stearyl alcohol; stearic acid; and mixtures of any two or more of the foregoing.

18. The dosage form of claim 12, wherein the active agent is an opioid agonist and the adverse agent is an opioid antagonist.

19. The dosage form of claim 18, wherein the opioid agonist is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, desomorphine, dextromoramide, dezocine, diampramide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

20. The dosage form of claim 19, wherein the opioid agonist is selected from the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

21. The dosage form of claim 18, wherein the opioid antagonist is selected from the group consisting of cyclazocine, naloxone, naltrexone, nalmeferine, nalbuphine, nalorphine, cyclazacine, levallorphan, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

22. The dosage form of claim 21, wherein the opioid antagonist is selected from the group consisting of nalmeferine, naloxone, naltrexone, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

23. The dosage form of claim 12, wherein the dosage form is an oral dosage form.

24. The dosage form of claim 23, wherein the dosage form comprises a capsule containing the first particles and the second particles.

25. The dosage form of claim 12, wherein the dosage form releases about 0.5 mg or less of the adverse agent *in vivo* following intact administration.

26. The dosage form of claim 25, wherein the dosage form releases about 0.05 mg or less of the adverse agent *in vivo* following intact administration.

5 27. An oral dosage form comprising:
a plurality of first particles comprising an opioid agonist;
a plurality of second particles comprising an adsorbent and an opioid
antagonist;
wherein at least a majority of the opioid agonist is adsorbed onto the
10 adsorbent; and
wherein the first particles provide a controlled release of the opioid
agonist upon oral administration to a patient.

15 28. The oral dosage form of claim 27, wherein the first particles and the
second particles each have a size of from about 0.1 mm to about 3.0 mm in any
dimension.

29. The oral dosage form of claim 27, wherein the second particles each
comprise at least one hydrophobic material disposed on at least a portion of the outer
surface of the adsorbent.

20 30. The oral dosage form of claim 29, wherein the at least one hydrophobic
material is selected from the group consisting of acrylic and methacrylic acid polymers
and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes,
fatty alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides,
hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon
25 backbones, and mixtures of any two or more of the foregoing.

31. The oral dosage form of claim 30, wherein the at least one hydrophobic
material is selected from the group consisting of glyceryl monostearate; beeswax; cetyl
alcohol; stearyl alcohol; hydrogenated castor oil; hydrogenated cottonseed oil; stearyl
alcohol; stearic acid; and mixtures of any two or more of the foregoing.

32. The oral dosage form of claim 27, wherein the opioid agonist is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metophon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

33. The oral dosage form of claim 32, wherein the opioid agonist is selected from the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

34. The oral dosage form of claim 27, wherein the opioid antagonist is selected from the group consisting of cyclazocine, naloxone, naltrexone, nalmeferine, nalbuphine, nalorphine, cyclazacine, levallorphan, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

35. The oral dosage form of claim 34, wherein the opioid antagonist is selected from the group consisting of naloxone, naltrexone and nalmeferine, pharmaceutically acceptable salts thereof, any mixtures of any two or more of the foregoing.

36. The oral dosage form of claim 27, wherein the dosage form comprises a tablet comprising the first particles and the second particles.

37. The oral dosage form of claim 27, wherein the dosage form comprises a capsule containing the first particles and the second particles.

38. The oral dosage form of claim 27, wherein the second particles release about 0.5 mg or less of the opioid antagonist *in vivo* following intact oral administration.

39. The oral dosage form of claim 38, wherein the second particles release about 0.05 mg or less of the opioid antagonist *in vivo* following intact oral
5 administration.

40. A dosage form comprising
an active agent;
an adsorbent; and
an adverse agent; wherein at least a majority of the adverse agent is
10 adsorbed onto the adsorbent.

41. The dosage form of claim 40, further comprising at least one hydrophobic material disposed on at least a portion of the outer surface of the adsorbent.

42. The oral dosage form of claim 41, wherein the at least one hydrophobic
15 material is selected from the group consisting of acrylic and methacrylic acid polymers and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes, fatty alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides, hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon backbones, and mixtures of any two or more of the foregoing.

20 43. The dosage form of claim 42, wherein the at least one hydrophobic material is selected from the group consisting of glyceryl monostearate; beeswax; cetyl alcohol; stearyl alcohol; hydrogenated castor oil; hydrogenated cottonseed oil; stearyl alcohol; stearic acid; and mixtures of any two or more of the foregoing. and mixtures of any two or more of the foregoing.

25 44. The dosage form of claim 40, wherein the active agent is an opioid agonist and the adverse agent is an opioid antagonist.

45. The dosage form of claim 44, wherein the opioid agonist is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine,
30 desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine,

dihydromorphine, dimenoxadol, dirnephheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, 5 lofentanil, meperidine, meptazinol, metazocine, methadone, metophon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, 10 tramadol, tilidine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

46. The dosage form of claim 45, wherein the opioid agonist is selected from the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, pharmaceutically acceptable salts 15 thereof, and mixtures of any two or more of the foregoing.

47. The dosage form of claim 44, wherein the opioid antagonist is selected from the group consisting of cyclazocine, naloxone, naltrexone, nalmeferene, nalbuphine, nalorphine, cyclazacine, levallorphan, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

20 48. The dosage form of claim 47, wherein the opioid antagonist is selected from the group consisting of nalmeferene, naloxone, naltrexone, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

49. The dosage form of claim 44, wherein the dosage form is an oral dosage form.

25 50. The dosage form of claim 44, wherein the dosage form comprises a capsule containing a plurality of particles.

51. The dosage form of claim 44, wherein the dosage form comprises a tablet.

52. The dosage form of claim 40, wherein the adsorbent comprises at least one material selected from the group consisting of activated charcoal, alumina, bentonite, kaolin, and mixtures of any two or more of the foregoing.

53. The dosage form of claim 52, wherein the adsorbent is activated charcoal.

5 54. The oral dosage form of claim 40, wherein the dosage form releases about 0.5 mg or less of the adverse agent *in vivo* following intact oral administration.

55. The oral dosage form of claim 54, wherein the dosage form releases about 0.05 mg or less of the adverse agent *in vivo* following intact oral administration.

10 56. The dosage form of claim 40, wherein the dosage form further comprises:
a core comprising the adsorbent and the adverse agent; and
a shell comprising the active agent;
wherein the shell surrounds a majority of the core.

15 57. A method for preparing a dosage form comprising:
providing an adsorbent;
providing a liquid comprising an adverse agent;
contacting the adsorbent with the liquid comprising the adverse agent for
sufficient time to allow at least a portion of the adverse agent to adsorb onto the
adsorbent;
20 separating the adsorbent from the liquid phase; and
optionally, washing the adsorbent.

58. The method of claim 57, wherein the adsorbent comprises at least one material selected from the group consisting of activated charcoal, alumina, bentonite, kaolin, and mixtures of and two or more of the foregoing.

25 59. The method of claim 57, further comprising applying at least one hydrophobic material to the outer surface of the adsorbent after removal of the adsorbent from the liquid phase.

60. The method of claim 59, wherein the at least one hydrophobic material is selected from the group consisting of acrylic and methacrylic acid polymers and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes, fatty

alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides, hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon backbones, and mixtures of any two or more of the foregoing.

61. The method of claim 57, wherein the adverse agent is an opioid antagonist.

62. The method of claim 61, further comprising adding the adsorbent and an opioid agonist to a dosage form.

63. A method for preparing a dosage form comprising:
providing an adsorbent;
providing a liquid comprising an adverse agent;
adding the adsorbent to a fluidized bed;
fluidizing the adsorbent;
spraying the liquid onto the fluidized adsorbent; and
optionally, drying the adsorbent.

64. The method of claim 63, wherein the adsorbent comprises at least one material selected from the group consisting of activated charcoal, alumina, bentonite, kaolin, and mixtures of and two or more of the foregoing.

65. The method of claim 63, further comprising applying at least one hydrophobic material to the outer surface of the adsorbent after removal of the adsorbent from the liquid phase.

66. The method of claim 65, wherein the at least one hydrophobic material is selected from the group consisting of acrylic and methacrylic acid polymers and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes, fatty alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides, hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon backbones, and mixtures of any two or more of the foregoing.

67. The method of claim 63, wherein the adverse agent is an opioid antagonist.

68. The method of claim 63, further comprising adding the adsorbent and an opioid agonist to a dosage form.

69. A method of treating a condition, or a symptom thereof, in a patient comprising administering to the patient a dosage form according to claim 40.

5 70. A method of treating a patient for pain comprising administering to the patient a dosage form according to claim 27.

71. A kit for treating a patient for pain comprising a dosage form according to claim 27, and instructions for directing the administration of the dosage form to the patient for the treatment of pain.